REMARKS

After entry of this amendment, claims 1-9 and 11-13, 15-25, and 27-29 are pending. Claims 14 and 26 were previously canceled. Claim 1 is amended. The amendment to claim 1 is supported, for example, by original claims 2 and 3.

35 U.S.C. § 112 Rejection

Reconsideration is respectfully requested of the rejection of claims 2-3, 5-9, and 23-24 under 35 U.S.C. § 112, second paragraph as failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The Office asserts that

> it is unclear how the subject matter of present claims 2-3, 5-9, and 23-24 are intended to further limit the parent claims from which they depend because each claim involves either administration prior to or simultaneously with the radiation exposure. However, the parent claims from which these claims depend each specifically require that the patient to whom the protective agent is to be administered has already previously been exposed to the radiation prior to the administration of the methionine compound.[1]

Contrary to the Office's assertion, claims 1 and 22 do not require that the patient already be exposed to radiation. Claims 1 and 22 merely require "a patient exposed to radiation for a time and at an intensity sufficient to result in alopecia." This claim element describes the time and intensity of the radiation by requiring that it be sufficient to result in alopecia. However, the broadest interpretation of this claim element does not require any temporal relationship between administration of the methionine protectant agent and the radiation exposure.

Further, claims 1 and 22 are directed to methods for treating alopecia. The definition of "treat" is to care for a patient medically or surgically.[2] When read in the context of the claims and specification as a whole, the meaning of treating alopecia is to administer the protective agent to a subject in need thereof; this administration could be prior to, simultaneous with or subsequent to the onset of alopecia. Thus, claims 1 and 22 encompass prophylactic administration prior to the onset of alopecia and such

[1] See Office action dated March 28, 2007 at page 3.
[2] Stedman's Medical Dictionary, 26th Ed., 1995.

administration serves to inhibit or control this condition. Accordingly, claims 2-3, 5-9, and 23-24 satisfy the requirements of the second paragraph of 35 U.S.C. § 112.

35 U.S.C. § 103 Rejection

Reconsideration is respectfully requested of the rejection of claims 1, 4, 11-13, 15-22, 25, and 27-29 under 35 U.S.C. § 103 as being unpatentable over Dye (U.S. Patent No. 5,122,369) in view of Jacobs et al. (Treatment of Radiation-Induced Alopecia, Head Neck Surg, 1979, 2(2), 154-159, abstract only).

The Dye reference relates to natural hair loss, not hair loss caused by treatment with radiation. For treating natural hair loss, Dye generally discloses various compositions comprising divalent iron and pantothenic acid along with racemic d,l-methionine. The reference also describes the stages of natural hair follicle growth and loss and relates the follicle stages to calcium concentration. For example, there are three phases in the natural hair loss cycle. The anagen phase is associated with active growth and high metabolic activity in the bulb region, the catagen phase is a transitory phase where the metabolic activity slows, and the telogen phase corresponds to a rest period followed by the hair follicle being pushed out by a new anagen hair. Dye described this three phase pilar cycle as depending on nutritional, endocrinal, and nervous (e.g., stress) factors.

According to Dye, the calcium concentration in the bulb of the hair generally increases across these stages, with the calcium concentration lowest in the anagen stage bulbs and highest in the telogen stage bulbs. Dye further states that "[t]hese observations have led to the development of a composition that has at least one active ingredient consisting essentially of active chelating agents"[3] and "the ability of such compositions to chelate divalent calcium ions is generally credited to be responsible for their efficacy."[4] The mechanism of hair loss described by Dye implies that by chelating or otherwise reducing the calcium concentration in the hair follicles, the natural progression to the telogen phase can be slowed or arrested. Generally, as Dye describes, follicles with higher calcium concentrations are closer to being lost.

[3] See Patent No. 5,122,369, column 2, lines 30-32.
[4] See Patent No. 5,122,369, column 2, lines 32-34.

However, there is no reference of record and applicant is unaware of any reference that would provide a reason that a person of skill would have believed that hair loss from causes other than the natural pilar cycle would also exhibit a similar calcium concentration profile. More particularly, there is no suggestion in Dye, or other art of record, that radiation would generate excessive calcium in the follicle bulbs. In fact, a literature reference describes the mechanism of hair loss induced by radiation as involving the p53 protein's effects on cell-cycle arrest and apoptosis in the follicular matrix.[5]

Jacobs et al. is directed to treatment of radiation-induced alopecia through a punch graft hair transplantation technique. While the abstract does state that radiation alopecia is a well-known complication of high-dosage radiotherapy, the abstract as a whole would have led a skilled person to conclude that hair transplantation was the best treatment approach.

Further, contrary to the Office's assertion, neither Dye nor Jacobs provides a reason to combine the disclosures. The Office's assertion picks the portion of the Jacobs abstract that states that alopecia is a well-known complication of high-dosage radiotherapy, but fails to mention that the abstract proposes a surgical hair transplantation solution to this problem. Thus, the Jacobs abstract as a whole would have led a person of skill in the art away from a chemical solution to radiation-induced alopecia. Further, Dye does not provide any reason that a skilled person would have believed that calcium levels would be affected by radiation, that methionine would materially affect calcium concentration in whatever range that calcium may appear during radiation treatment, or that controlling the calcium concentration in the hair follicles would affect radiation-induced alopecia. Thus, contrary to the Office's assertion, there would not have been a reasonable expectation that the Dye composition would be effective as a protectant for alopecia arising from radiation exposure as required by claims 1 and 22. In sum, claims 1 and 22, and the claims that depend therefrom are patentable over Dye in view of Jacobs et al. under 35 U.S.C. § 103(a).

[5] Song et al., *Am J. Pathology* **1999**, *155(4)*, 1121-1127.

The Claimed Methods are Not *prima facie* Obvious in View of the Claims of the Cited Patents.

Reconsideration is requested of the rejection of claims 1-9 and 11-29 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 35 and 36 of U.S. Patent No. 6,187,817.

The analysis employed in an obvious-type double patenting rejection parallels the guidelines of a 35 U.S.C. § 103 obviousness determination.[6] However, an important distinction exists. A rejection for obviousness must be based on a comparison of the claimed invention to the entirety of the disclosure in the prior art reference, whereas an obviousness-type double patenting rejection must be grounded on a comparison of the claimed invention to the claims, **and only the claims**, of the reference.[7]

It is respectfully submitted that the subject matter of the claims of the present application would not have been obvious in view of claims 35 and 36 of U.S. Patent Nos. 6,187,817. When evaluating the scope of a claim, every element of the claim must be considered.[8] To support an obviousness-type double patenting rejection, the claims must have been obvious at the time of filing and not merely obvious upon hindsight reconstruction using applicant's disclosure as a template to arrive at the features of the instantly claimed methods from the claims of the '817 patent. It is respectfully submitted that the Office has failed to establish obviousness based on this reference, or by evidence of the level of skill in the art or the nature of the problem, that is not based upon impermissible hindsight reconstruction.

U.S. Patent Application No. 11/539,975

Claims 1-9 and 11-29 of the instant application are directed to methods for treating alopecia in a patient exposed to radiation, the method comprising administering to said patient an effective amount of a methionine protective agent. Claim 17 of the '975 application is directed to the use of a combination that can include a methionine protectant

[6] In re Braat, 937 F.2d 589 (Fed. Cir. 1991).
[7] Purdue Pharma L.P. v. Boehringer Ingelheim GMbH, 98 F.Supp.2d 362, 392, 55 USPQ2d 1168, 1190 (S.D.N.Y. 2000), *aff'd*, 237 F.3d 1359, 57 USPQ2d 1647 (Fed. Cir. 2001).
[8] See, e.g., In re Ochiai, 71 F.3d 1565, 1572, 37 USPQ2d 1127, 1133 (Fed. Cir. 1995).

agent for a variety of insults. The filing date of the '975 application is October 10, 2006, while the filing date of the instant application is October 27, 2003. Therefore, since the filing date of the instant application is earlier, once the instant application is otherwise in condition for allowance, this double patenting rejection should be withdrawn because the instant application is earlier filed.[9]

U.S. Patent No. 6,187,817

The claims of the instant application are described above. Claims 35-36 of the '817 patent are directed to methods of preventing or reducing alopecia arising from treatment with a chemotherapeutic effective amount of an anti-tumor platinum-coordination compound. Accordingly, because claims 35 and 36 of the '817 patent are not directed to protection of toxicities arising from radiation exposure, the claims do not include all the elements of the subject claims.

However, without conceding the propriety of the rejection, a terminal disclaimer is filed herewith.

[9] M.P.E.P. § 804.

CONCLUSION

Applicant submits that the present application is now in a condition for allowance and requests early allowance of the pending claims.

The Commissioner is hereby authorized to charge any underpayment and credit any overpayment of government fees to Deposit Account No. 19-1345.

Respectfully submitted,

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JSH/dep